REMARKS/ARGUMENTS

After entry of this amendment, claims 42-46 and 51-54 are pending, claims 46 and 50 having been canceled and claims 51-54 having been added. Support for the amendment to claim 42 is provide at, *e.g.*, p. 19 line 1 of the specification. Support for new claims 51-54 is provide at, *e.g.*, p. 17 lines 1-8 of the specification.

Rejection of Claims 42-48 and 50 Under the Doctrine of Obviousness Type Double Patenting

It is the Examiner's position that claims 48-48 and 50 are unpatentable over the claims of U.S. 6, 284,221 in light of Vigo-Pelfrey et al because it would have been obvious to screen for soluble Aβ(x-≥ 41) in place of soluble Aβ because Aβ(x-≥ 41) is a recognized soluble species of Aβ. Without agreeing with the basis of this rejection, Applicants have amended independent claim 42 to recite "wherein the amount of Aβ(x-≥ 41) is measured by exposing the cerebral spinal fluid to an antibody or fragment thereof specific for an epitope of Aβ(x-≥ 41) but that does not cross react with an epitope of Aβ(x-≤40)."

The diagnostic method disclosed in U.S. 6,284,221 (the '221 patent) relies on the discovery that the presence of the Aβ-related condition will generally be associated with elevated levels of Aβ in a patient's body fluid when compared to those values in normal individuals, *i.e.*, individuals not suffering from Alzheimer's disease or any other Aβ-related condition. The diagnostic methods of the '221 patent and the present invention rely on different diagnostic indicators. The method of the '221 patent correlates high levels of soluble Aβ with Alzheimer's disease, while the present invention correlates Aβ (x-≥ 41) in amounts that are in the very low end of the normal range with Alzheimer's disease. The disclosure of the '221 patent does not suggest that one of skill in the art would expect to find levels Aβ (x-≥ 41) in amounts which are in the very low end of the normal range present in the CSF of non-Alzheimer's individuals.

Vigo-Pelfrey et al. discuss the use of the monoclonal 226 antibody, which is raised against Aβ13-28, to isolate and characterize of multiple complex forms of Aβ from CSF. Aβ species containing 27, 28, 30, 35, 40, 42, and 43 amino acids were identified using laser desorption mass spectrometry. Vigo-Pelfrey et al. discuss neither a screening method nor a

method to distinguish between Aβ (x-≥ 41) and Aβ (x-≤ 40). Vigo-Pelfrey et al. do not appreciate the discovery which the present invention relies on, at least in part, *i.e.*, that the cerebrospinal fluid (CSF) of individuals suffering from Alzheimer's disease generally contains Aβ (x-≥ 41) in amounts which are in the very low end of the normal range present in the CSF of non-Alzheimer's individuals. The Aβ species identified by Vigo-Pelfrey et al. do not suggest that one of skill in the art would expect to find levels Aβ (x-≥ 41) in amounts which are in the very low end of the normal range present in the CSF of non-Alzheimer's individuals.

The disclosure of Vigo-Pelfrey et al. would not prompt the skilled person to modify or adapt the '221 patent to arrive at the presently claimed invention. The present invention results at least in part from the discovery that the cerebrospinal fluid (CSF) of individuals suffering from Alzheimer's disease generally contains Aβ (x-≥ 41) in amounts which are in the very low end of the normal range present in the CSF of non-Alzheimer's individuals. This discovery is new and surprising because elevated levels of Aβ42 in body fluids are associated with Alzheimer's disease, and because the bulk of Aβ deposits in the brain tissue of persons suffering from Alzheimer's disease is Aβ42. Without the knowledge of the discovery of the present invention, a skilled person would not have modified or adapted the diagnostic method disclosed in the '221 patent with the Aβ species identified by Vigo-Pelfrey et al.

Rejection of Claim 46 Under 35 U.S.C. § 112, First Paragraph

Claim 46 has been canceled to expedite prosecution without conceding that the Examiner's rejection under 35 U.S.C. § 112, first paragraph is warranted.

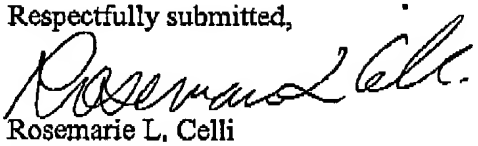
Objection to Claim 50

Claim 50 has been canceled, thus mooting the objection.

All amendments are for purposes of expediting prosecution and should not be construed as an acquiescence in any ground of rejection.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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